Letter to the Editor

Use of ondansetron for food protein–induced enterocolitis syndrome

To the Editor:

Food protein–induced enterocolitis syndrome (FPIES) is a non–IgE-mediated food allergy characterized by severe, repetitive vomiting that begins about 2 hours after the ingestion of the problem food.[1-3] Diarrhea may also occur, and reactions typically result in acute dehydration, frequently with hypotension, shock, acidemia, and methemoglobinemia. FPIES usually resolves in the first 5 years of life, and medically supervised oral food challenges are the primary means of determining whether a child has outgrown this allergy. The etiology of FPIES is not well understood, but it is thought to result from food-antigen–induced elaboration of proinflammatory cytokines by intestinal lymphocytes, resulting in increased intestinal permeability, malabsorption, and dysmotility.

Oral food challenges in patients with FPIES are typically performed with intravenous access in place because reactions often evolve rapidly and fluid resuscitation is the primary mode of treatment. Intravenous corticosteroids are also often recommended to decrease the presumed intestinal inflammation.[1,3] While symptoms typically resolve over a period of 2 to 4 hours, some reactions are more prolonged and the profound nature of the vomiting leads to considerable discomfort to the child, stress and anxiety for the family, and sometimes dehydration even with intravenous access in place.

Ondansetron hydrochloride is a highly potent and selective serotonin 5-HT3 receptor antagonist that is approved for use in preventing and treating nausea and vomiting induced by chemotherapy and radiation, with a low risk of adverse effects.[4] Recently, ondansetron has been used successfully off-label in emergency room settings to control vomiting, such as in acute gastroenteritis.[5,6] Significant side effects are uncommon and unlike other antiemetics, ondansetron does not have the safety concerns of excessive drowsiness or extrapyramidal reactions, although special caution may be warranted in children with underlying heart disease, as QT prolongation has been observed.

Here we report the rapid resolution of FPIES reactions in 5 consecutive patients undergoing oral food challenges in our Pediatric Allergy Clinic at Johns Hopkins Hospital who were treated with ondansetron. The oral challenge details were as follows:

- Patient 1 was a 7-year-old girl, weight 23.5 kg, who had a convincing history of a FPIES reaction to wheat. Two hours after the ingestion of 1 serving of wheat, she acutely developed profuse vomiting with pallor, confusion, and lethargy. She was administered 3.5 mg of ondansetron intravenously, along with normal saline fluid replacement. Her vomiting and other symptoms resolved within 15 minutes of infusion. She was monitored for another 2 hours with no return of symptoms.
- Patient 2 was a 5-year-old boy, weight 20 kg, with a history of FPIES to peanut. One and one-half hours after ingesting 5 g of peanut protein, he developed profuse vomiting with pallor and irritability. He was administered 2 mg of oral dissolvable ondansetron along with normal saline fluid replacement. He experienced slight improvement in symptoms after 30 minutes, but continued with severe abdominal pain and diarrhea and was given 2 mg of ondansetron intravenously. He experienced resolution of all symptoms within 10 minutes of infusion.
- Patient 3 was a 3-year-old boy, weight 12.8 kg, with a history of FPIES to egg. Two hours after the ingestion of approximately 4 g of egg protein, he developed profuse vomiting and irritability. He was administered 2 mg of ondansetron intravenously along with normal saline fluid replacement. He experienced resolution of all symptoms within 10 minutes of infusion. An hour later, the vomiting recurred, although not as severely as initially, and he was given 1 mg of ondansetron intravenously with complete resolution of symptoms within 30 minutes.
- Patient 4 was a 12-year-old boy, weight 50 kg, with a history of FPIES to milk. He had had 3 prior milk challenges since the age of 3 years, all resulting in severe vomiting treated with fluid resuscitation and intravenous hydrocortisone sodium succinate with resolution over 4 to 6 hours. In this challenge, 2½ hours after the ingestion of 8 g of milk protein he developed profuse vomiting, pallor, and abdominal pain. He was administered 4 mg of ondansetron intravenously along with fluid replacement with resolution of all symptoms 15 minutes after infusion.
- Patient 5 was a 10-year-old boy, weight 27.6 kg, with a history of FPIES to rice. Two hours and 15 minutes after eating a serving of rice, he developed profuse vomiting, pallor, abdominal pain, and lethargy. He was given 4 mg of ondansetron intravenously along with fluid replacement and had complete resolution of symptoms within 10 minutes of infusion.

While still anecdotal, these cases suggest that ondansetron may have great value in treating FPIES reactions during oral food challenges, and possibly with FPIES reactions outside of the food challenge setting. This series is not a subset of responders but rather represents 5 consecutive cases, and no nonresponders have yet been identified. As noted, most FPIES reactions take 2 to 4 hours to resolve and in the over 100 adverse FPIES reactions personally witnessed over the years in our food challenge clinic, we have never seen any patient's symptoms resolve in less than an hour. In addition to relieving the severe discomfort associated with these reactions, ondansetron may prevent the more serious sequelae of FPIES, including dehydration and shock. In addition, although based on a single case, intravenous ondansetron may be more effective than the oral preparation.

It is important to recognize that the mechanism by which ondansetron exerts its beneficial effect in FPIES reactions is not completely clear. Ondansetron acts on serotonin receptors both peripherally and centrally, and its benefit in chemotherapy-induced vomiting is thought to be through inhibition of serotonin receptors on vagal nerve afferents that initiate the vomiting reflex. Whether the effects of ondansetron are mediated centrally or peripherally, if the efficacy of ondansetron in FPIES reactions is confirmed, these findings may help shed light on the poorly understood pathophysiology of FPIES reactions. In addition, the apparent efficacy of ondansetron raises questions as to whether

inflammation is truly the central mechanism underlying FPIES, as has been previously suggested, and whether corticosteroids truly have a role in the treatment of FPIES reactions. In this series, no patient was treated with corticosteroids, or even intravenous fluids once symptoms had resolved.

Further study is clearly warranted, but on the basis of the dramatic effects seen in this small case series, we would recommend that ondansetron be routinely used in the treatment of FPIES reactions, both in the food challenge setting and in the emergency room.

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